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Description

9

Claim(s)

4

Abstract

1

Drawing(s)

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Powder loading method

5

Field of invention

10 This invention relates to a method and apparatus for loading blind cavities with powder. This invention has particular application to the situation where the blind cavities are defined by the blisters of blister packs.

Background to the invention

15

The use of blister packs to hold medicaments for inhalation devices, for example in bronchodilation therapy, is well known. The blister packs usually consist of a base strip in which blisters are formed. The blisters are arranged on the base sheet and can be filled with medicament to be administered through use of an
20 inhalation device. A lid sheet is applied to cover the filled blisters and the two sheets are sealed together to form a blister pack.

25

There can, however, be problems associated with methods of filling the blisters with powdered medicament. Powder, particularly the drug component of the powder, can tend to be attracted to the base sheet surface rather than to the blister pockets. This attraction of the drug to the base sheet can result in
inaccurate filling of the blisters, create mess and potentially cause problems with adherence of the lid sheet to the base sheet. Such processes may also require a large reservoir of powder, potentially resulting in waste of the medicament.

30

The Applicants have now found that the potential problem of powder adherence can be overcome by using a filling method utilising a perforated plate to mask the base sheet surface during filling to avoid covering this area with powder. The

perforated plate is simply moved into contact with the appropriate areas of the blister strip during filling and then moved away at the end of the process and can be reused in each cycle. This filling method, therefore, aims to prevent the powder adhering to the blister strip, rather than relying on using processes such as additional cleaning steps to remove the powder after it has accumulated.

The perforated plate is also used to assist with ensuring the correct dose of powder is loaded into the blind cavity. In one aspect, adjusting the size of the perforation enables different doses to be loaded into the blisters.

US 5,187,921 describes a method and apparatus for filling a blind cavity, for example a blister of a blister pack, with a quantity of powder.

Summary of the invention

According to the invention there is provided a method of loading a blind cavity with a quantity of powder which comprises:

- a) closing off a perforation in a perforated plate;
- b) directing powder into said closed-off perforation;
- c) compacting said powder in the closed-off perforation;
- d) re-opening the perforation;
- e) placing a blind cavity in registration with the perforation; and
- f) transferring the powder from the perforation to said blind cavity.

Preferably the closing-off is achievable by the use of a blanking plate. The blanking plate is positioned so that it is in contact with the perforated plate.

Alternatively the closing-off is achievable by the use of a blanking pin inserted into the perforation.

Preferably the blanking pin is moveable within the perforation to adjust the volume of the closed-off perforation.

Preferably the compacting is achievable by the use of a compacting pin. The compacting pin is inserted into the closed-off perforation.

The invention further provides a method of loading a blind cavity with a quantity of powder which comprises:

- 5 a) closing off a perforation in a perforated plate by placing a blind cavity in registration with the perforation;
- b) directing powder into said closed-off perforation;
- c) transferring said powder from the perforation into said blind cavity.

10 Preferably the powder is directable by the action of a sweeping leveller blade into the perforations. Sometimes a thin layer of excess powder is left on the surface of the perforated plate.

Preferably the powder is transferable by the action of a transfer pin.

- 15 In one aspect, direction of powder into the closed-off perforation and transfer into the blind cavity is a continuous step.

An additional component of the invention comprises removing excess powder from the perforated plate subsequent to directing powder into the perforation.

20

Preferably the excess powder is removable by the action of a wiper blade. The wiper blade moves in close proximity to the surface of the perforated plate to ensure that excess powder is not transferred to the blind cavity.

- 25 An additional component of the invention comprises compacting the powder in the blind cavity.

Preferably the powder is compactable by the action of a compacting pin.

- 30 Preferably the transfer pin and the compacting pin are integral.

More preferably the transfer pin and the compacting pin are identical. The pin is inserted into the perforation, transferring the powder through to the blind cavity and the pin then compacts the powder in the cavity following completion of
35 transfer.

Preferably the blind cavity is a blister pocket. The blister pocket may be part of an elongate blister strip used in inhalation devices.

5 An additional component of the invention comprises applying a lid to the blind cavity to protect the powder therein.

Preferably the powder comprises a medicament selected from the group consisting of albuterol, salmeterol, fluticasone propionate and beclomethasone dipropionate and salts or solvates thereof and any mixtures thereof.

10 The invention also provides an apparatus for loading a blind cavity with a quantity of powder, which comprises:

- a) a perforated plate;
- b) a closure for reversibly closing off a perforation in said perforated plate; and
- 15 c) a director for directing powder into said perforation;
- d) a compactor for compacting powder in the perforation;
- e) an aligner for aligning said blind cavity with the perforation; and
- f) a transferor for transferring powder from the perforation into the blind cavity.

20 Preferably the closure comprises a blanking plate.

Alternatively the closure comprises a blanking pin inserted into the perforation.

25 Preferably the blanking pin is moveable within the perforation to adjust the volume of the perforation.

Alternatively the closure comprises a base sheet comprising said blind cavity.

30 Preferably the director comprises a sweeping leveller blade.

Preferably the compactor comprises a compactor pin.

Preferably the transferor comprises a transfer pin.

35 Preferably the transferor and compactor are integral.

More preferably the transferor and compactor are identical.

An additional component of the invention comprises a powder remover for removing excess powder from the perforated plate subsequent to action of the powder director.

Preferably the powder remover comprises a wiper blade.

An additional component of the invention comprises a lid applier for applying a lid to the blind cavity to protect the powder therein.

Brief Description of the Drawings

The invention will now be described with reference to the accompanying drawings in which:

FIG 1a shows the first stage in a filling process in accord with the present invention;

FIG 1b shows a subsequent stage in the filling process of Fig 1a;

FIG 1c shows a second subsequent stage in the filling process of Fig 1a;

FIG 2a shows the first stage in a second filling process in accord with the present invention;

FIG 2b shows a subsequent stage in the second filling process of Figure 2a; and

FIG 3 shows the first stage in a third filling process in accord with the present invention.

Detailed Description of the Drawings

Fig 1a shows the first stage in a filling process herein. A perforated plate 10 in contact with a blanking plate 20 creates closed-off perforations 12a, 12b. On the opposite side of the perforated plate 10 to the blanking plate 20 is a reservoir of powder 30. The powder 30 comprises a suitable medicament formulation. The powder 30 is directed into the perforations 12a, 12b by the action of a sweeping leveller blade 40 which moves horizontally across the powder reservoir 30 and moves the powder 30 along the length of the perforated plate 10 leaving a thin layer of excess powder 32 still in contact with the perforated plate 10. A wiper

blade 50, for example of stainless steel or rubber, follows the sweeping leveller blade 40 and moves along the powder reservoir 30 in close proximity to the surface of the perforated plate 10, removing the excess powder 32 from the perforated plate surface 10.

5

Figure 1b shows an optional subsequent stage in which compaction pins 70a, 70b are inserted into the closed-off perforations 12a, 12b to compact the powder 30 held within the perforation 12a, 12b. The compaction pins 70a, 70b are then removed from the perforations 12a, 12b and this is followed by removal of the
10 blanking plate 20 from its position in contact with the perforated plate 10. The powder 30 generally has poor flow properties and therefore remains in the perforations 12a, 12b.

Figure 1c shows a further stage in which a blister strip 60 is moved so that it is
15 positioned with the blister pockets 62a, 62b in line with the perforations 12a, 12b and the base sheet 64 is masked by the solid sections 14a, 14b of the perforated plate 10. The transfer and compaction pins 70a, 70b are inserted through the perforated plate 10 and the powder 30 is transferred to the blister pockets 62a, 62b. The filled blister strip 60 is then lowered and the pins 70a, 70b raised.

20

The blanking plate 20 is relocated against the underside of the perforated plate 10, creating closed off perforations 12a, 12b, which are filled with powder 30 in the next cycle.

25 Figure 2a shows an alternative filling process. A perforated plate 110 is positioned so that the blister pockets 162a, 162b of a blister strip 160 are in registration with the perforations 112a, 112b in the plate 110. The solid areas 114a, 114b of the perforated plate 110 mask the base sheet 164 of the blister strip 160.

30

On the opposite side of the perforated plate 110 to the blister strip 160 is a reservoir of powder 130. The powder 130 is made up of the drug and a suitable excipient. The powder 130 is then directed into the perforations 112a, 112b by the action of a sweeping leveller blade 140. The sweeping leveller blade 140
35 moves horizontally across the powder reservoir 130 and moves the excess powder 132 along the length of the perforated plate 110 leaving a thin layer of

powder 132 still in contact with the perforated plate 110. A wiper blade 150, for example of stainless steel or rubber, follows the sweeping leveller blade 140 and moves along the powder reservoir 130 in close proximity to the surface of the perforated plate 110, removing excess powder 132 from the perforated plate surface 110.

Figure 2b shows a subsequent stage in which transfer and compaction pins 170a, 170b are inserted through the perforated plate 110 forcing the powder 130 through into the underlying blister pockets 162a, 162b and compacting the powder 130 in the pockets 162a, 162b. The pins 170a, 170b are raised and the blister strip 160 moves ready for the next section to be filled with powder 130 by the action of the sweeping leveller blade 140.

Fig 3 shows the first stage in an alternative filling process herein. Blanking pins 280a, 280b are inserted into a perforated plate 210 to create closed-off perforations 212a, 212b. The volume of the closed-off perforations 212a, 212b may be varied by varying the insertion depth of the blanking pins 280a, 280b. On the opposite side of the perforated plate 210 to the blanking pins 280a, 280b is a reservoir of powder 230. The powder 230 comprises a suitable medicament formulation. The powder 230 is directed into the perforations 212a, 212b by the action of a sweeping leveller blade 240 which moves horizontally across the powder reservoir 230 and moves the powder 230 along the length of the perforated plate 210 leaving a thin layer of excess powder 232 still in contact with the perforated plate 210. A wiper blade 250, for example of stainless steel or rubber, follows the sweeping leveller blade 240 and moves along the powder reservoir 230 in close proximity to the surface of the perforated plate 210, removing the excess powder 232 from the perforated plate surface 210.

This first stage of the process shown in Fig 3 is then followed by a compaction stage as in Figure 1b, followed by removal of the blanking pin from the perforations, and then continues with transfer of the powder into a blister strip as shown in Figure 1c.

The blister strip may be sealed by applying a lid sheet and providing sealing means so that the powder is contained in a medicament container defined by the pocket and elongate strip. Suitable methods of sealing the medicament carrier

include the use of adhesives, staples or stamps and welding methods selected from hot metal welding, radio frequency welding and ultrasonic welding. Such sealing techniques may be used to form a suitable seal around the periphery of the medicament pocket which is capable of being peeled away by the patient or
5 by a suitable trigger release mechanism in a controlled manner when in use.

The invention is suitable for filling blister packs with powdered medicament, particularly for the treatment of respiratory disorders. Appropriate medicaments may thus be selected from, for example, analgesics, e.g., codeine,
10 dihydromorphine, ergotamine, fentanyl or morphine; anginal preparations, e.g., diltiazem; antiallergics, e.g., cromoglycate, ketotifen or nedocromil; anti-infectives e.g., cephalosporins, penicillins, streptomycin, sulphonamides, tetracyclines and pentamidine; antihistamines, e.g., methapyrilene; anti-inflammatory, e.g., beclomethasone dipropionate, fluticasone propionate, flunisolide, budesonide,
15 rofleponide, mometasone furoate or triamcinolone acetonide; antitussives, e.g., noscapine; bronchodilators, e.g., albuterol, salmeterol, ephedrine, adrenaline, fenoterol, formoterol, isoprenaline, metaproterenol, phenylephrine, phenylpropanolamine, pirbuterol, reproterol, rimiterol, terbutaline, isoetharine, tulobuterol, or (-)-4-amino-3,5-dichloro- α -[[[6-[2-(2-pyridinyl)ethoxy] hexyl]methyl]
20 benzenemethanol; diuretics, e.g., amiloride; anticholinergics, e.g., ipratropium, tiotropium, atropine or oxitropium; hormones, e.g., cortisone, hydrocortisone or prednisolone; xanthines, e.g., aminophylline, choline theophyllinate, lysine theophyllinate or theophylline; therapeutic proteins and peptides, e.g., insulin or glucagon. It will be clear to a person skilled in the art that, where appropriate, the
25 medicaments may be used in the form of salts, (e.g., as alkali metal or amine salts or as acid addition salts) or as esters (e.g., lower alkyl esters) or as solvates (e.g., hydrates) to optimise the activity and/or stability of the medicament.

Preferred medicaments are selected from albuterol, salmeterol, fluticasone propionate and beclomethasone dipropionate and salts or solvates thereof, e.g.,
30 the sulphate of albuterol and the xinafoate of salmeterol.

Medicaments can also be delivered in combinations. Preferred formulations containing combinations of active ingredients contain salbutamol (e.g., as the free
35 base or the sulphate salt) or salmeterol (e.g., as the xinafoate salt) in combination

with an anti-inflammatory steroid such as a beclomethasone ester (e.g., the dipropionate) or a fluticasone ester (e.g., the propionate).

5 It will be understood that the present disclosure is for the purpose of illustration only and the invention extends to modifications, variations and improvements thereto.

10 The application of which this description and claims form part may be used as a basis for priority in respect of any subsequent application. The claims of such subsequent application may be directed to any feature or combination of features described therein. They may take the form of product, method or use claims or may include, by way of example and without limitation, one or more of the following claims.

CLAIMS

- 5 1. A method of loading a blind cavity with a quantity of powder which comprises:
a) closing off a perforation in a perforated plate;
b) directing powder into said ~~closed-off perforation~~;
c) compacting said powder in the ~~closed-off perforation~~;
d) re-opening the perforation;
10 e) placing a blind cavity in registration with the perforation; and
f) transferring the powder from the perforation to said blind cavity.
- 15 2. A method according to claim 1, wherein the closing-off is achievable by the use of a blanking plate.
3. A method according to claim 1, wherein the closing off is achievable by the use of a blanking pin inserted into the perforation.
- 20 4. A method according to claim 3, wherein the blanking pin is moveable within the perforation to adjust the volume of the ~~closed-off perforation~~.
5. A method according to any of ~~claims 1 to 4~~, wherein the compacting is achievable by the use of a ~~compacting pin~~.
- 25 6. A method of loading a blind cavity with a quantity of powder which comprises:
a) closing off a perforation in a perforated plate by placing a blind cavity in registration with the perforation;
b) directing powder into said closed-off perforation; and
c) transferring said powder from the perforation into said blind cavity.
- 30 7. A method according to any of claim 1 to 6, wherein the powder is directable by the action of a ~~sweeping leveller blade~~.
- 35 8. A method according to any of ~~claims 1 to 7~~, wherein the powder is transferable ~~by the action of a transfer pin~~.

9. A method according to either of claims 7 and 8 wherein direction of powder into the closed-off perforation and transfer into the blind cavity is a continuous step.

5 10. A method according to either any of claims 1 to 9, additionally comprising removing excess powder from said perforated plate subsequent to directing powder into the perforation.

10 11. A method according to claim 10, comprising removing said excess powder by the action of a wiper blade.

12. A method according to any of claims 1 to 11, additionally comprising compacting the powder in the blind cavity.

15 13. A method according to claim 12, wherein the powder is compactable by the action of a compacting pin.

14. A method according to any of claims 1 to 13, wherein the transfer pin and the compacting pin are integral.

20 15. A method according to any of claims 1 to 13, wherein the transfer pin and the compacting pin are identical.

25 16. A method according to any of claims 1 to 15, wherein the blind cavity is a blister pocket.

17. A method according to any of claims 1 to 16, additionally comprising applying a lid to the blind cavity to protect the powder therein.

30 18. A method according to any of claims 1 to 17, wherein the powder comprises a medicament selected from the group consisting of albuterol, salmeterol, fluticasone propionate and beclomethasone dipropionate and salts or solvates thereof and any mixtures thereof.

19. An apparatus for loading a blind cavity with a quantity of powder, which comprises:
 - a) a perforated plate;
 - 5 b) a closure for reversibly closing off a perforation in said perforated plate;
 - c) a director for directing powder into said perforation;
 - f) a compactor for compacting powder in the perforation;
 - g) an aligner for aligning said blind cavity with the perforation; and
 - f) a transferor for transferring powder from the perforation into the blind
10 cavity.
20. An apparatus according to claim 19, wherein the closure comprises a blanking plate.
- 15 21. An apparatus according to claim 19, wherein the closure comprises a blanking pin inserted into the perforation.
22. An apparatus according to claim 21, wherein the blanking pin is moveable within the perforation to adjust the volume of the perforation.
- 20 23. An apparatus according to claim 19, wherein the closure comprises a base sheet comprising said blind cavity.
24. An apparatus according to any of claims 19 to 23, wherein the director
25 comprises a sweeping leveller blade.
25. An apparatus according to any of claims 19 to 23, wherein the compactor comprises a compactor pin.
- 30 26. An apparatus according to any of claims 19 to 25, wherein the transferor comprises a transferor pin.
27. An apparatus according to either of claims 25 or 26, wherein the transferor and compactor are integral.

35

28. An apparatus according to either of claims 25 or 26, wherein the transferor and compactor are identical.
- 5 29. An apparatus according to any of claims 19 to 28, additionally comprising a powder remover for removing excess powder from the perforated plate subsequent to action of the powder director.
- 10 30. An apparatus according to claim 29, wherein the powder remover comprises a wiper blade.
31. An apparatus according to any of claims 19 to 30, additionally comprising a lid applier for applying a lid to the blind cavity to protect the powder therein.
- 15 32. An apparatus, substantially as hereinbefore described with reference to and as illustrated in the accompanying drawings.

Abstract

A method of loading a blind cavity with a quantity of powder which comprises: closing off a perforation in a perforated plate; directing powder into the closed-off perforation; 5 compacting the powder in the closed-off perforation; re-opening the perforation; placing a blind cavity in registration with the perforation; and transferring the powder from the perforation to the blind cavity.

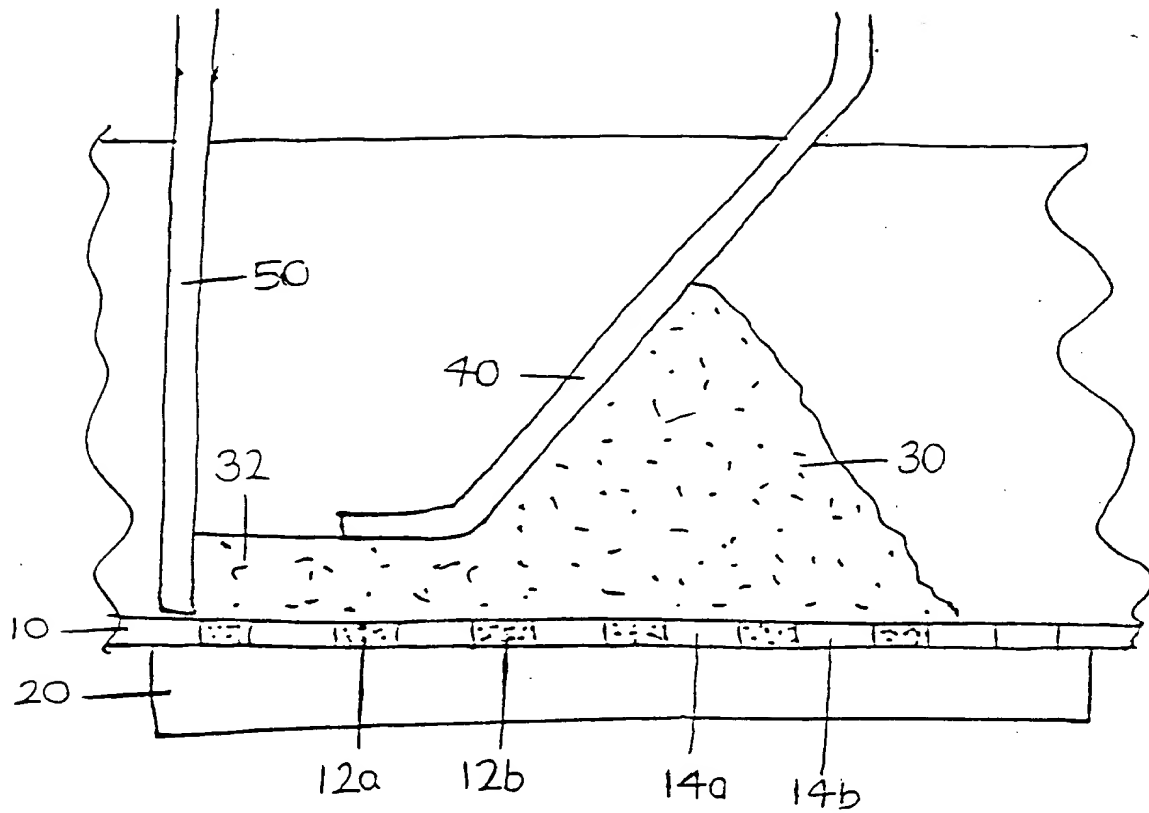


Figure 1a

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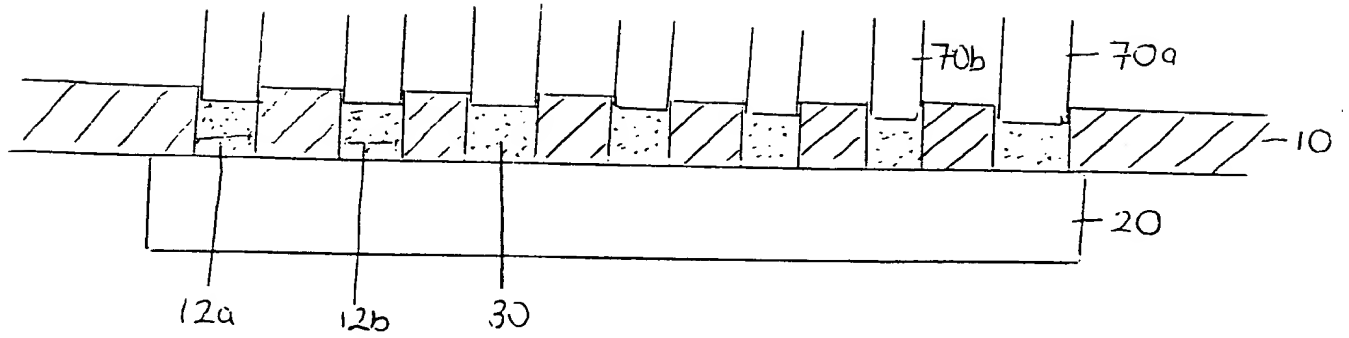


Figure 1b

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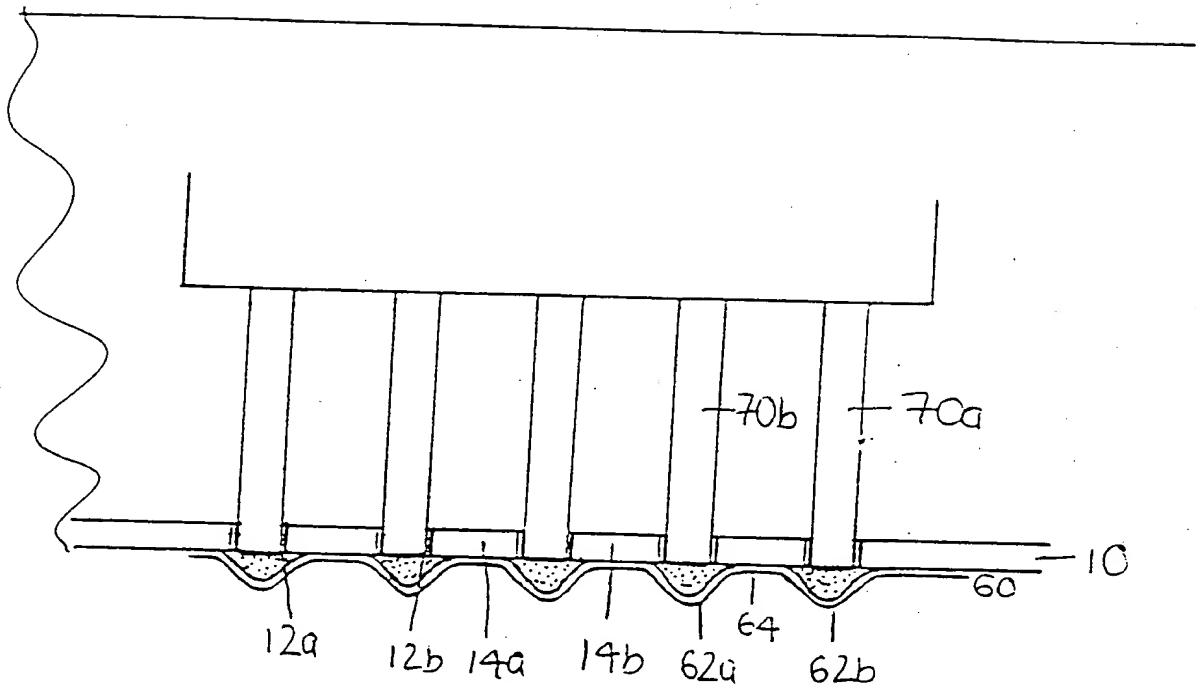


Figure 1c

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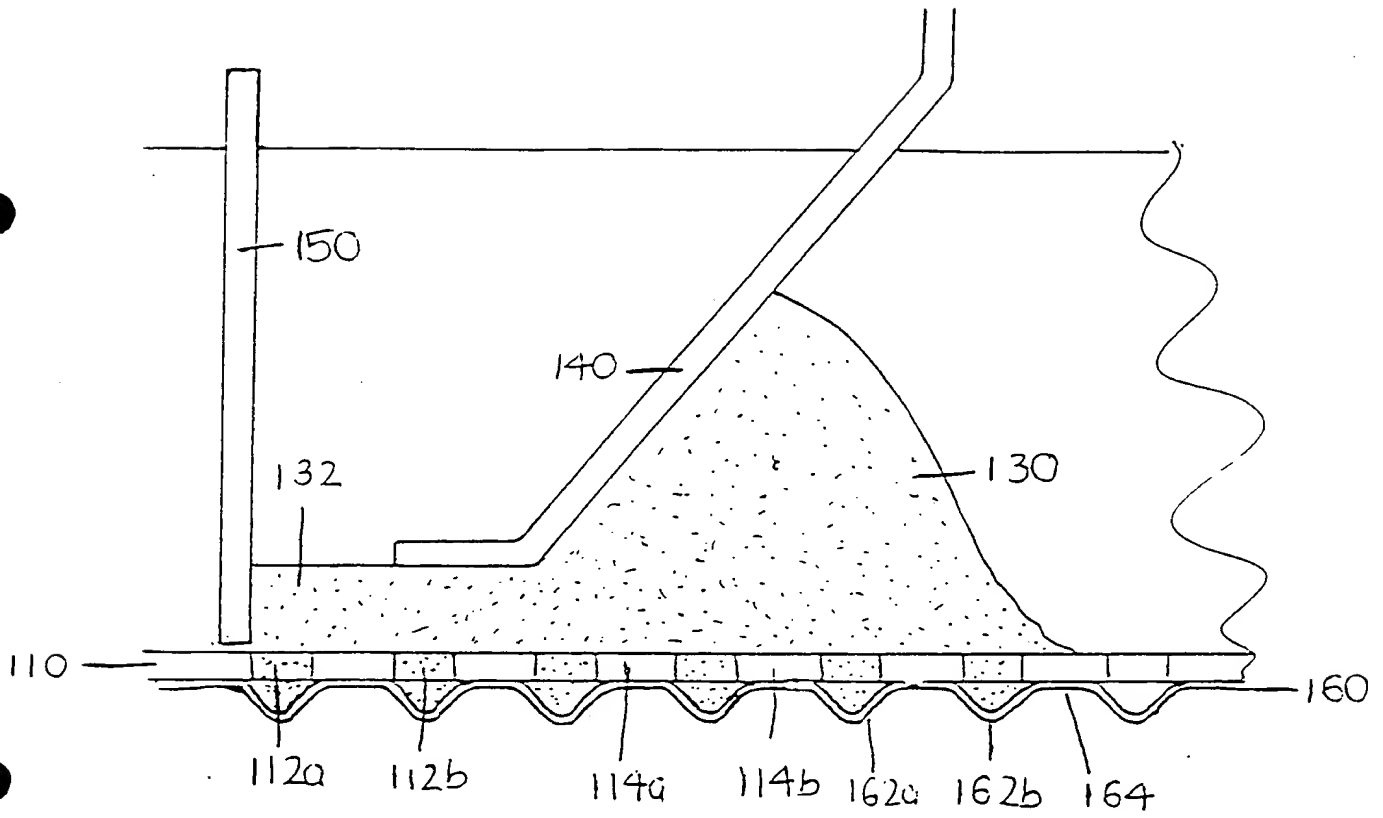


Figure 2a

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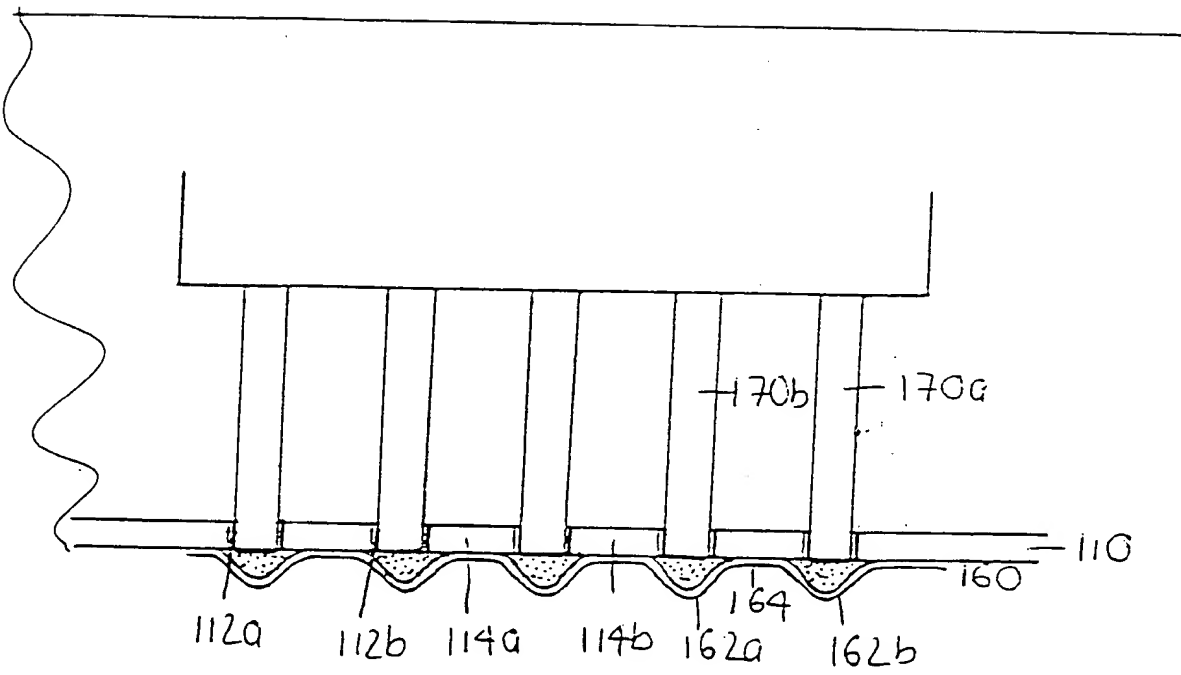


Figure 2b.

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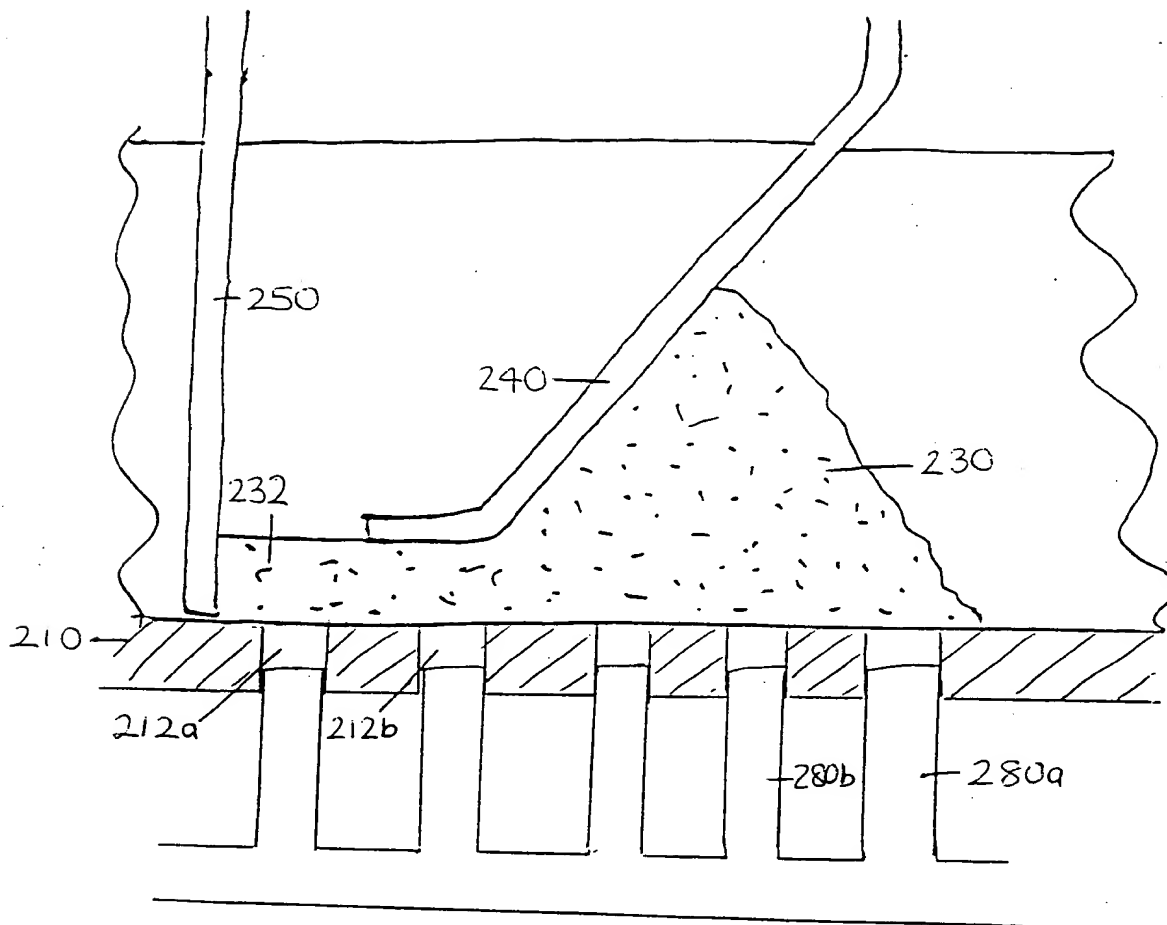


Figure 3

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